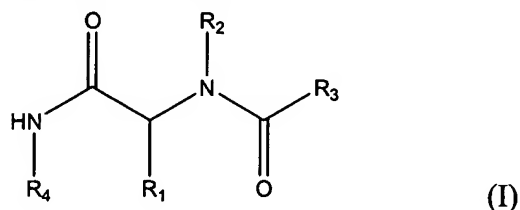


CLAIMS

What is claimed is:

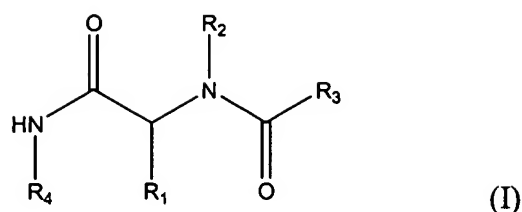
- 5 1. A method of inhibiting tissue transplant rejection in a subject with a tissue transplant, said method comprising the step of administering an effective amount of a compound represented by Formula (I):



or a physiological salt thereof, wherein:

- 10 R_1 is a substituted or unsubstituted aryl group or a substituted or unsubstituted alkyl group;
- R_2 is an optionally substituted aralkyl group or an alkyl group substituted with $-NR_5R_6$;
- 15 R_3 is a substituted or unsubstituted alkyl group or a substituted or unsubstituted aryl group;
- R_4 a substituted or unsubstituted alkyl group or a substituted or unsubstituted aryl group; and
- 20 R_5 and R_6 are independently selected from a substituted or unsubstituted alkyl group or a substituted or unsubstituted aryl group or R_5 and R_6 taken together with the nitrogen to which they are attached are a non-aromatic heterocyclic group.
- 25 2. A method of inhibiting chronic tissue transplant rejection in a subject with a tissue transplant, said method comprising the step of administering an effective amount of a compound represented by Formula (I):

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or a physiological salt thereof, wherein:

R_1 is a substituted or unsubstituted aryl group or a substituted or unsubstituted alkyl group;

5 R_2 is an optionally substituted aralkyl group or an alkyl group substituted with $-NR_5R_6$;

R_3 is a substituted or unsubstituted alkyl group or a substituted or unsubstituted aryl group;

10 R_4 a substituted or unsubstituted alkyl group or a substituted or unsubstituted aryl group; and

R_5 and R_6 are independently selected from a substituted or unsubstituted alkyl group or a substituted or unsubstituted aryl group or R_5 and R_6 taken together with the nitrogen to which they are attached are a non-aromatic heterocyclic group.

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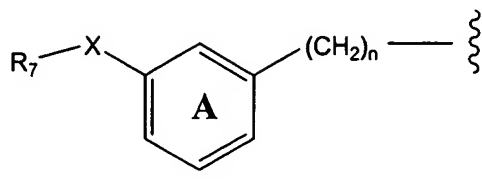
3. The method of Claim 2 wherein R_2 is an optionally substituted heteroaralkyl group or an alkyl group substituted with $-NR_5R_6$.

20 4. The method of Claim 3 wherein R_4 is an optionally substituted aryl group, an optionally substituted cycloalkyl group, an optionally substituted C_1 - C_4 aralkyl group or an optionally substituted C_1 - C_4 cycloalkylalkyl group.

25 5. The method of Claim 4 wherein R_4 is an optionally substituted phenyl group, an optionally substituted phenyl- C_1 - C_4 -alkyl group, an optionally substituted diphenyl- C_1 - C_4 -alkyl group, an optionally substituted C_3 - C_8 -cycloalkyl- C_1 - C_4 -alkyl group or an optionally substituted di- $(C_3$ - C_8 -cycloalkyl)- C_1 - C_4 -alkyl group.

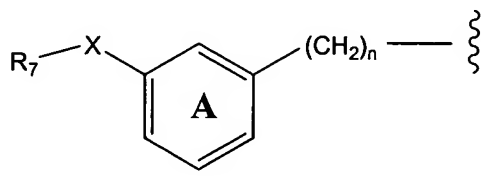
6. The method of Claim 5 wherein R₄ is an optionally substituted benzyl, an optionally substituted diphenylmethyl, an optionally substituted 2-phenylethyl, an optionally substituted 1,2-diphenylethyl, an optionally substituted 2,2-diphenylethyl or an optionally substituted 3,3-diphenylpropyl.
7. The method of Claim 3 wherein R₁ is an optionally substituted aryl group or an optionally substituted C₁-C₄ aralkyl group.
8. The method of Claim 7 wherein R₁ is an optionally substituted phenyl group or an optionally substituted phenyl-C₁-C₄ alkyl group.
9. The method of Claim 3 wherein R₃ is an optionally substituted aryl group or an optionally substituted C₁-C₄ aralkyl group.
10. The method of Claim 9 wherein R₃ is an optionally substituted phenyl, an optionally substituted phenyl-C₁-C₄-alkyl, an optionally substituted diphenyl-C₁-C₄-alkyl, an optionally substituted pyrazolyl, an optionally substituted pyrazolyl-C₁-C₄-alkyl, an optionally substituted indolyl, an optionally substituted indolyl-C₁-C₄-alkyl, thienylphenyl, thienylphenyl-C₁-C₄-alkyl, furanylphenyl, furanylphenyl-C₁-C₄-alkyl, an optionally substituted fluorenyl, an optionally substituted fluorenyl-C₁-C₄-alkyl, an optionally substituted naphthyl, an optionally substituted naphthyl-C₁-C₄-alkyl, an optionally substituted quinoxaliny, an optionally substituted quinoxaliny-C₁-C₄-alkyl, an optionally substituted quinazoliny, an optionally substituted quinazoliny-C₁-C₄-alkyl, an optionally substituted pyrrolyl, an optionally substituted pyrrolyl-C₁-C₄-alkyl, an optionally substituted thienyl, an optionally substituted thienyl-C₁-C₄-alkyl, an optionally substituted furanyl, an optionally substituted furanyl-C₁-C₄-alkyl, an optionally substituted pyridyl or an optionally substituted-C₁-C₄ pyridyl.

11. The method of Claim 10 wherein R_3 is represented by the following structural formula:



- wherein Ring A substituted or unsubstituted; R_7 is an optionally substituted phenyl, optionally substituted furanyl, optionally substituted thienyl or optionally substituted pyridyl group; n is an integer from 1-4; and X is a bond, CH_2 , OCH_2 , $CH_2OC(O)$, CO , $OC(O)$, $C(O)O$, O , S , SO or SO_2 .
12. The method of Claim 3 wherein R_3 is an optionally substituted an optionally substituted 2-cyclohexylethyl, an optionally substituted 2-cyclopentylethyl, or an optionally substituted C_3 - C_8 secondary or tertiary alkyl group.
13. The method of Claim 3 wherein R_2 is an optionally substituted 2-(imidazol-4-yl)ethyl, an optionally substituted 3-(imidazol-4-yl)propyl, an optionally substituted 3-(imidazol-1-yl)propyl, an optionally substituted 2-(morpholin-4-yl)ethyl, an optionally substituted 2-(4-pyrazolyl)ethyl, an optionally substituted 2-*N,N*-dimethylaminoethyl or an optionally substituted 3-*N,N*-dimethylaminopropyl.
14. The method of Claim 3 wherein:
- R_1 is an optionally substituted aryl group or an optionally substituted C_1 - C_4 aralkyl group;
 - R_3 is an optionally substituted aryl group or an optionally substituted C_1 - C_4 aralkyl group; and
 - R_4 is an optionally substituted aryl group, an optionally substituted cycloalkyl group, an optionally substituted C_1 - C_4 aralkyl group or an optionally substituted C_1 - C_4 cycloalkylalkyl group.

15. The method of Claim 3 wherein:
- a) R_1 is an optionally substituted phenyl group or an optionally substituted phenyl- C_1 - C_4 alkyl group;
 - 5 b) R_3 a substituted or unsubstituted phenyl, phenyl- C_1 - C_4 -alkyl, diphenyl- C_1 - C_4 -alkyl, pyrazolyl, pyrazolyl- C_1 - C_4 -alkyl, indolyl, indolyl- C_1 - C_4 -alkyl, thienylphenyl, thienylphenyl- C_1 - C_4 -alkyl, furanylphenyl, furanylphenyl- C_1 - C_4 -alkyl, fluorenyl, fluorenyl- C_1 - C_4 -alkyl, naphthyl, naphthyl- C_1 - C_4 -alkyl, quinoxaliny, quinoxaliny- C_1 - C_4 -alkyl, an optionally substituted
10 quinoxaliny, an optionally substituted quinoxaliny- C_1 - C_4 -alkyl, pyrrolyl, pyrrolyl- C_1 - C_4 -alkyl, thienyl, thienyl- C_1 - C_4 -alkyl, furanyl or furanyl- C_1 - C_4 -alkyl; and
 - c) R_4 is an optionally substituted phenyl group, an optionally substituted phenyl- C_1 - C_4 -alkyl group, an optionally substituted diphenyl- C_1 - C_4 -alkyl
15 group, an optionally substituted C_3 - C_8 -cycloalkyl- C_1 - C_4 -alkyl group or an optionally substituted di- $(C_3$ - C_8 -cycloalkyl)- C_1 - C_4 -alkyl group.
16. The method of Claim 15 wherein R_2 is an optionally substituted imadazolyl- C_1 - C_4 -alkyl group or a C_1 - C_4 alkyl group substituted with $-NR_5R_6$.
- 20 17. The method of Claim 16 wherein R_3 is represented by the following structural formula:

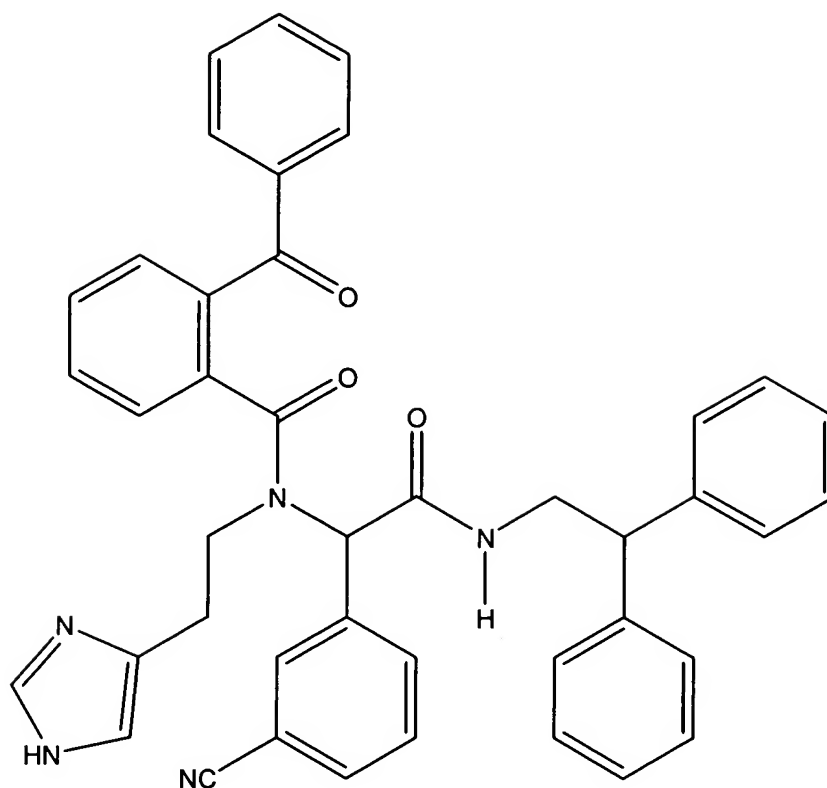


- 25 wherein Ring A substituted or unsubstituted; R_7 is an optionally substituted phenyl, furanyl, thienyl or pyridyl group; n is an integer from 1-4; and X is a bond, CH_2 , OCH_2 , $CH_2OC(O)$, CO , $OC(O)$, $C(O)O$, O , S , SO or SO_2 .

18. The method of Claim 17 wherein R_4 is 2,2-diphenylethyl, 2-phenylethyl, benzyl, diphenylmethyl, 1,2-diphenylethyl, 3,3-diphenylpropyl, benzyl, or 2-pyridylethyl, each optionally substituted with -OH, halogen, R, -CH₂R, -OCH₂R, -CH₂OC(O)R, -OR, -O-COR, -COR, -CN, -NO₂, -COOH, -SO₃H, -NH₂, -NHR, -N(R)₂, -COOR, -CHO, -CONH₂, -CONHR, -CON(R)₂, -NHCOR, -NRCOR, -NHCONH₂, -NHCONRH, -NHCON(R)₂, -NRCONH₂, -NRCONRH, -NRCON(R)₂, -C(=NH)-NH₂, -C(=NH)-NHR, -C(=NH)-N(R)₂, -C(=NR)-NH₂, -C(=NR)-NHR, -C(=NR)-N(R)₂, -NH-C(=NH)-NH₂, -NH-C(=NH)-NHR, -NH-C(=NH)-N(R)₂, -NH-C(=NR)-NH₂, -NH-C(=NR)-NHR, -NH-C(=NR)-N(R)₂, -NRH-C(=NH)-NH₂, -NR-C(=NH)-NHR, -NR-C(=NH)-N(R)₂, -NR-C(=NR)-NH₂, -NR-C(=NR)-NHR, -NR-C(=NR)-N(R)₂, -SO₂NH₂, -SO₂NHR, -SO₂N(R)₂, -SH or -SO_kR;
- each R is independently C₁-C₄ alkyl or phenyl optionally substituted with amino, alkylamino, dialkylamino, aminocarbonyl, halogen, alkyl, alkylaminocarbonyl, dialkylaminocarbonyloxy, alkoxy, nitro, cyano, carboxy, alkoxycarbonyl, alkylcarbonyl, hydroxy, haloalkoxy, or haloalkyl; and
- k is zero, one or two.
19. The method of Claim 18 wherein R_1 is a phenyl group or phenyl-C₁-C₄ alkyl group each optionally substituted with R, -CH₂R, -OCH₂R, -CH₂OC(O)R, -OH, halogen, -OR, -O-COR, -COR, -CN, -NO₂, -COOH, -SO₃H, -NH₂, -NHR, -N(R)₂, -COOR, -CHO, -CONH₂, -CONHR, -CON(R)₂, -NHCOR, -NRCOR, -NHCONH₂, -NHCONRH, -NHCON(R)₂, -NRCONH₂, -NRCONRH, -NRCON(R)₂, -C(=NH)-NH₂, -C(=NH)-NHR, -C(=NH)-N(R)₂, -C(=NR)-NH₂, -C(=NR)-NHR, -C(=NR)-N(R)₂, -NH-C(=NH)-NH₂, -NH-C(=NH)-NHR, -NH-C(=NH)-N(R)₂, -NH-C(=NR)-NH₂, -NH-C(=NR)-NHR, -NH-C(=NR)-N(R)₂, -NRH-C(=NH)-NH₂, -NR-C(=NH)-NHR, -NR-C(=NH)-N(R)₂, -NR-C(=NR)-NH₂, -NR-C(=NR)-NHR, -NR-C(=NR)-N(R)₂, -SO₂NH₂, -SO₂NHR, -SO₂N(R)₂, -SH or -SO_kR.

20. The method of Claim 19 wherein R_1 is a phenyl group or phenyl- C_1 - C_2 alkyl group, each optionally substituted with C_1 - C_4 alkyl, C_1 - C_4 alkoxy, halogen, CN, C_1 - C_4 -alkylthiol, C_1 - C_4 -haloalkyl or phenoxy; R_4 is 2,2-diphenylethyl, 2-phenylethyl, benzyl, diphenylmethyl, 1,2-diphenylethyl, 3,3-diphenylpropyl, benzyl, or 2-pyridylethyl, each optionally substituted with C_1 - C_4 alkyl, C_1 - C_4 alkoxy, halogen, CN, C_1 - C_4 -alkylthiol, C_1 - C_4 -haloalkyl or phenoxy; R_7 is an optionally substituted phenyl group; n is 1; and X is CO.
21. The method of Claim 20 wherein Ring A is unsubstituted and R_7 is a phenyl group optionally substituted with R, $-CH_2R$, $-OCH_2R$, $-CH_2OC(O)R$, $-OH$, halogen, $-OR$, $-O-COR$, $-COR$, $-CN$, $-NO_2$, $-COOH$, $-SO_3H$, $-NH_2$, $-NHR$, $-N(R)_2$, $-COOR$, $-CHO$, $-CONH_2$, $-CONHR$, $-CON(R)_2$, $-NHCOR$, $-NRCOR$, $-NHCONH_2$, $-NHCONRH$, $-NHCON(R)_2$, $-NRCONH_2$, $-NRCONRH$, $-NRCON(R)_2$, $-C(=NH)-NH_2$, $-C(=NH)-NHR$, $-C(=NH)-N(R)_2$, $-C(=NR)-NH_2$, $-C(=NR)-NHR$, $-C(=NR)-N(R)_2$, $-NH-C(=NH)-NH_2$, $-NH-C(=NH)-NHR$, $-NH-C(=NH)-N(R)_2$, $-NH-C(=NR)-NH_2$, $-NH-C(=NR)-NHR$, $-NH-C(=NR)-N(R)_2$, $-NRH-C(=NH)-NH_2$, $-NR-C(=NH)-NHR$, $-NR-C(=NH)-N(R)_2$, $-NR-C(=NR)-NH_2$, $-NR-C(=NR)-NHR$, $-NR-C(=NR)-N(R)_2$, $-SO_2NH_2$, $-SO_2NHR$, $-SO_2N(R)_2$, $-SH$ or $-SO_kR$.
22. The method of Claim 21 wherein R_7 is a phenyl group.
23. The method of Claim 22 wherein R_2 is 2-(imidazol-4-yl)ethyl.
24. A method of inhibiting tissue transplant rejection in a subject with a tissue transplant, said method comprising the step of administering an effective amount of a compound represented by the following structural formula:

-28-

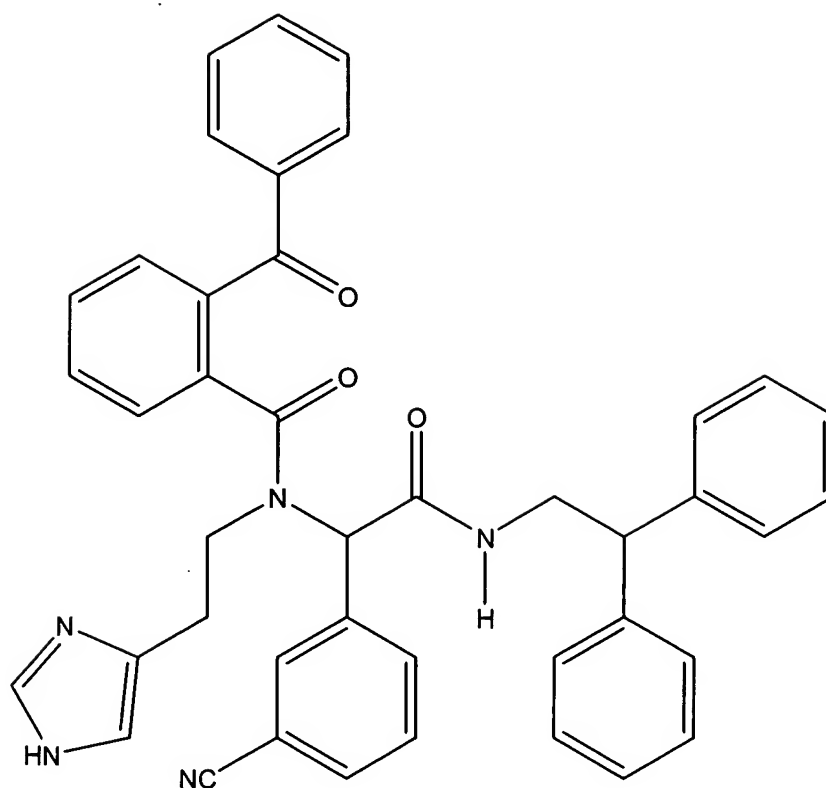


or a pharmaceutically acceptable salt thereof.

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25. A method of inhibiting chronic tissue transplant rejection in a subject with a tissue transplant, said method comprising the step of administering an effective amount of a compound represented by the following structural formula:

-29-



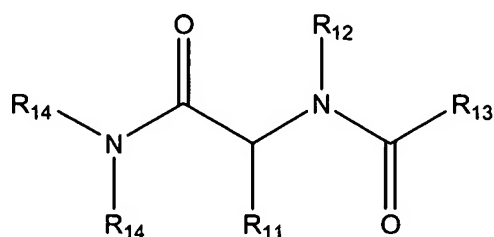
(II).

or a pharmaceutically acceptable salt thereof.

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26. A method of inhibiting tissue transplant rejection in a subject with a tissue transplant, said method comprising the step of administering an effective amount of a compound represented by the following structural formula:

10



or a physiologically acceptable salt thereof, wherein:

R_{11} is -H, a substituted or unsubstituted aryl, a substituted or unsubstituted aralkyl, a substituted or unsubstituted heteroaryl or a substituted or unsubstituted heteroaralkyl;

5 R_{12} is alkyl substituted with $NR_{15}R_{16}$, a substituted or unsubstituted aryl, a substituted or unsubstituted heteroaralkyl, or a substituted or unsubstituted heterocycloalkylalkyl;

10 R_{13} is a substituted or unsubstituted alkyl, a substituted or unsubstituted aryl, a substituted or unsubstituted aralkyl, a substituted or unsubstituted cycloalkylalkyl, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted heteroaralkyl, a substituted or unsubstituted benzophenonyl, or a substituted or unsubstituted cycloalkylalkyl; and

15 each R_{14} is independently, -H, a substituted or unsubstituted alkyl, a substituted or unsubstituted aryl, substituted or unsubstituted aralkyl or a substituted or unsubstituted heteroaralkyl;

R_{15} and R_{16} are independently selected from H, a substituted or unsubstituted alkyl, a substituted or unsubstituted cycloalkyl, a substituted or unsubstituted aryl or unsubstituted aralkyl or R_{13} and R_{14} together with the nitrogen to which they are attached are a heterocycloalkyl.